

REMARKS

Status of the Claims

Claims 1-35 are pending. Claims 11-13 and 15-35 are withdrawn.
Claims 1-10 and 14 are rejected.

Claim 1, 2, 3, 4 and 6 are amended and claims 8, 11-13 and 15-35 are canceled herein. No new matter is added herein.

Claim Amendments

Claim 1 is amended to overcome the 35 U.S.C. §102(b) and §103(a) rejections. Amended claim 1 is directed to a chimeric mouse/human monoclonal antibody. Such an antibody comprises a chimeric heavy chain and chimeric light chain. The sequence of the chimeric heavy chain comprises a human immunoglobulin heavy chain constant domain sequence and a heavy chain variable domain sequence of a murine antibody. Similarly, the sequence of the chimeric light chain comprises a human immunoglobulin light chain constant domain sequence and a light chain variable domain sequence of a murine antibody. Furthermore, the heavy chain variable domain sequence and the light chain variable domain sequence also comprise a leader sequence. The chimeric mouse/human monoclonal antibody claimed herein is supported by the teachings of the instant invention (pg 24, lines 10-16; pg 24, line 27-pg. 25, line 17).

Claims 2, 3, 4 and 6 are amended to properly depend from amended claim 1. Amended claim 2 limits the human immunoglobulin heavy chain constant domain sequence to the constant domain sequence of human IgG heavy chain and the human immunoglobulin light chain constant domain sequence to sequence of constant domain of human kappa light chain. Amended claim 3 further limits the constant domain sequence of human IgG heavy chain to human IgG2 heavy chain constant domain sequence or to human IgG4 heavy chain constant domain sequence. The amended claim 4 limits the amino acid sequence of the chimeric light chain to SEQ ID NO: 16 and amended claim 6 limits the amino acid sequence of the chimeric heavy chain to SEQ ID NO: 18. Additionally, claim 8 is canceled herein to overcome the rejection for being indefinite. Furthermore, claims 11-13 and 15-35 that were withdrawn are canceled herein.

The 35 U.S.C. §112, Second Paragraph, Rejection

Claim 8 is rejected under 35 U.S.C §112, second paragraph as being indefinite. Applicant respectfully traverses this rejection.

The Examiner states that claim 8 is indefinite in its recitation of ch-mAb6B5 because its characteristics are not known. The Examiner states that ch-mAb6B5 is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct antibodies.

Claim 8 is canceled herein. Accordingly, Applicant submits that the rejection of claim 8 under 35 U.S.C. §112, second paragraph rejection is moot.

The 35 U.S.C. §102 Rejection

Claims 1-3 and 14 are rejected under 35 U.S.C. §102 (b) as being anticipated by **U.S. Patent No: 6,358,710 B1**. Applicant respectfully traverses this rejection.

The Examiner states that the **U.S. Patent No: 6,358,710B1** teaches a chimeric antibody derived from monoclonal antibody of human and murine origins (col. 7, lines 4-25). The Examiner further states that the **U.S. Patent No: 6,358,710 B1** teaches the use of human constant regions of IgG2, IgG4 as heavy chain and kappa for light chain, respectively (col. 7, lines 10-15) and administering the antibody with drugs or clearing agent (i.e. pharmaceutically acceptable carrier, col. 8, lines 46-67). Based on this, the Examiner states that the prior art anticipates the claimed invention.

Claim 1 is amended to recite the components of the chimeric mouse/human monoclonal antibody as discussed *supra*. As per this amendment, both the heavy chain variable domain sequence of the murine antibody and the light chain variable domain sequence of the murine antibody comprises a leader sequence. As discussed *supra*, the claimed antibody is supported by the teachings of the instant invention.

In order to anticipate a claim, the prior art reference must teach and every element of the claim. The prior art reference (**U.S. Patent No: 6,358,710**)

cited herein does not teach inclusion of a leader sequence in the chimeric mouse/human monoclonal antibody. Hence, **U.S. Patent No: 6,358,710** does not anticipate claim 1. Since claim 14 is dependent from the amended claim 1, it is not anticipated by the prior art either. Accordingly based on the claim amendments and above-discussed remarks, Applicant respectfully requests the withdrawal of rejection of claims 1-3 and 14 under 35 U.S.C. §102(b).

The 35 U.S.C. §103 Rejection

Claims 1-10 and 14 are rejected under 35 U.S.C. §103(a) as being unpatentable over **Hardin et al** (J Pharm Exp Ther., 285:1113-1122, 1998) as is evidenced by **Lim et al** (J Biol Chem, 273(44): 28576-28582, 1998) and **U.S. Patent No: 6,358,710** in view of **McLean et al** (Mol Imm 37:837-845, 2000). Applicant respectfully traverses this rejection.

The Examiner states that **Hardin et al** teach the murine monoclonal antibody mAb6B5 Fab (abstract, p. 1114 under Materials and Methods) binds to phencyclidine and **Lim et al** disclose the complete sequences of mAb6B5 heavy chain and light chain (fig. 1). Additionally, the Examiner states that it is well-known in the antibody therapy art to develop a humanized antibody to reduce immunogenicity (**U.S. Patent No: 6,358,710**, col. 1, lines 35-50). Furthermore, the Examiner states that although **Hardin et al** do not teach chimeric murine and human antibodies, **McLean et al** teach various human expression vectors associated with IgG1, IgG2, IgG3, IgG4 and kappa chain constant regions. These expression vectors are constructed to include promoter sequences, leader

sequences (2.3-2.5, Fig. 1, 2), drug resistant marker and VDJ cassette, which can be replaced with any variable region of interest (p. 841, 2.7). Additionally, these expression vectors are easy to manipulate by replacing various variable regions (i.e. Fab of mAb6B5) to produce functional Ig proteins (p. 843, 3.3) and can be used in transfection to generate Ig antibodies (2.5). Therefore, the Examiner concludes that one of ordinary skill in the art would have been motivated to combine the variable region of murine mAb6B5 Fab taught by **Hardin et al** and **Lim et al** in the expression cassette with built in human constant heavy and light chain regions taught by **McLean et al** to create therapeutically more important chimeric antibody and produce functional Ig.

Claim 1 has been amended as discussed supra and recites inclusion of leader sequence in the heavy chain variable domain sequence and the light chain variable domain sequence. This amendment is supported by the teachings of the instant invention as discussed supra. The cited prior art references combined do not teach or suggest the inclusion of such leader sequences in the construction of a chimeric mouse/human monoclonal antibody. Infact, comparison of the heavy chain and light chain variable regions of the antibody taught in **Lim et al** (Fig. 1) differ from the sequence disclosed in the instant invention. Thus, Applicant submits that the prior art references combined do not teach or suggest all elements of the amended claim.

For the same reason, Applicant further submits that even if one of ordinary skill in the art were motivated to combine the teachings of the prior art references as suggested by the Examiner, one would not arrive be able to arrive

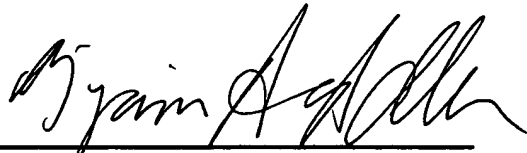
at the instantly claimed monoclonal antibody with reasonable expectation of success. Thus, the invention as a whole was not prima facie obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, based on the claim amendments and remarks, Applicant respectfully requests the withdrawal of rejection of claims 1-10 and 14 under 35 U.S.C. §103(a).

This is intended to be a complete response to the Office Action mailed February 22, 2006. Applicant submits that the pending claims are in condition for allowance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted

Date: _____

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